

IN THE CLAIMS

Please amend the claims as follows:

Claim 1 (Withdrawn): A method for evolving an X protein encoded by a *Lactobacillus fermentum* (*L. fermentum*) *ntd* gene to modify its characteristics, comprising the following steps:

- a) obtaining mutants of the *L. fermentum ntd* gene by random mutagenesis;
- b) transforming cells comprising a [P-] phenotype with vectors comprising the mutated nucleic acid obtained in step a) coding for the thus modified X\* proteins, P-meaning that said cells are auxotrophic for the substance P, P being the product of the action of X on its natural substrate S;
- c) culturing said cells in a medium comprising a substrate S\*,  
S\* being an analogue of the natural substrate S of said X protein; and
- d) selecting the cells [P-:: X\*] that have survived step c) in which the X\* proteins are capable of carrying out the biosynthesis of the product P from the substrate S\*.

Claim 2 (Withdrawn): The method according to claim 1, wherein the mutant X\* protein obtained is a protein possessing an activity similar to said protein X, i.e. belonging to the same or adjacent enzyme classes having at least the first three figures 2.4.2 of the EC 4-figure international nomenclature classes.

Claim 3 (Withdrawn): The method according to claim 1, wherein the cells used in step b) are obtained by the inactivation of at least one gene involved in the natural metabolic pathway leading to the product P.

Claim 4 (Withdrawn): The method according to claim 3, wherein the protein X\* complements the deficiency of the natural metabolic pathway leading to the product P in a medium provided with the substrate S\*.

Claim 5 (Withdrawn): The method according to claim 1, wherein the activity of the protein X on the substrate S is at least two times greater than its activity on the substrate S\*.

Claim 6 (Withdrawn): The method according to claim 1, wherein the activity of the protein X\* on the substrate S\* is at least 10 times greater than its activity on the substrate S.

Claim 7 (Withdrawn): The method according to claim 1, wherein the random mutagenesis of step a) is carried out either by variation of the manganese concentration during the PCR reaction, or by the use of promutagenic nucleotide analogues or also by the utilization of primers comprising a random sequence.

Claim 8 (Withdrawn): The method according to claim 1, wherein said cells are prokaryotic or eukaryotic cells, preferably *E. coli*.

Claim 9 (Withdrawn): The method according to claim 1, wherein an N-deoxyribosyl transferase (DTP) of *L. fermentum* is evolved to obtain a protein is an N-dideoxyribosyl transferase by the following steps:

- a) obtaining DTP\* mutants of the sequence coding for an N-deoxyribosyl transferase (DTP) by random mutagenesis;
- b) transforming cells comprising an [N-] phenotype with vectors comprising the mutated nucleic acid obtained in step a) coding for the DTP\* proteins, N- meaning that said

cells are auxotrophic for at least one nucleoside, said nucleoside being the product of the action of DTP on its natural substrate dR-N;

- c) culturing said cells in a medium comprising a ddR-N substrate; and
- d) selecting the [N-:: DTP\*] cells that have survived step c) in which the DTP\* proteins are capable of carrying out the transfer of the dideoxyribose (ddR) from a dideoxyribonucleoside to another nucleoside leading to the production of the N nucleoside necessary for the survival of the cells.

Claim 10 (Withdrawn): The method according to claim 9 wherein the (ntd) sequence encoding the N-deoxyribosyl transferase (DTP) of *L. fermentum* corresponds to SEQ ID No. 1 which is being evolved.

Claim 11 (Withdrawn): The method according to claim 9, wherein the cells used in step b) are bacteria of genotype  $\Delta pyrC$ ,  $\Delta codA$ ,  $\Delta cdd$  deficient in the metabolic pathway leading to uracil.

Claim 12 (Withdrawn): The method according to claim 11, wherein the bacteria of genotype  $\Delta pyrC$ ,  $\Delta codA$ ,  $\Delta cdd$  deficient in the metabolic pathway leading to uracil used are *E. coli*.

Claim 13 (Currently Amended): A ~~N-deoxyribosyl transferase~~ protein (DTP) that has at least 90% identity with the polypeptide of SEQ ID NO: 2 or SEQ ID NO: 4, but which is not SEQ ID NO: 2; that retains residues Y13, D77, D97, E103, and [[M312]] M132 that respectively correspond to positions 13, 77, 97, 103, and 132 of SEQ ID NO: 2; and

that has threonine at a position corresponding to position 15 of SEQ ID NO: 2 or SEQ ID NO: 4.

Claim 14 (Previously Presented): The protein according to claim 13, which is at least 95% identical with SEQ ID NO: 2.

Claim 15 (Previously Presented): The protein according to claim 13 which is at least 95% identical to SEQ ID NO: 4.

Claim 16 (Currently Amended): The protein according to claim 13, which is at least [[95%]] 98% identical to SEQ ID NO: 4.

Claim 17 (Currently Amended): The protein according to claim 13, which comprises SEQ ID NO: 2, ~~but which does not consist of~~ provided said protein is not a protein consisting of the amino acid sequence of SEQ ID NO: 2.

Claim 18 (Previously Presented): The protein according to claim 13, which comprises SEQ ID NO: 4.

Claims 19-20 (Cancelled)

Claim 21 (Previously Presented): The protein according to claim 13, which has a N-dideoxyribosyl transferase activity.

Claim 22 (Previously Presented): The protein according to claim 13, wherein said protein has a deoxyribose and dideoxyribose and/or didehydroribose transfer activity.

Claim 23 (Previously Presented): The protein according to claim 13, wherein said protein has a catalytic activity on d4T and ddT greater than that of the native N-deoxyribosyl transferase protein of *L. fermentum* represented by SEQ ID NO: 2.

Claim 24 (Previously Presented): The protein according to claim 23, wherein said catalytic activity on d4T and ddT is 50% greater than that of the native N-deoxyribosyl transferase protein of *L. fermentum* represented by SEQ ID NO: 2.

Claim 25 (Previously Presented): The protein according to claim 13, wherein said protein has a catalytic effectiveness on d4T and ddT greater than that of the native N-deoxyribosyl transferase protein of *L. fermentum* represented by SEQ ID NO: 2.

Claim 26 (Previously Presented): The protein according to claim 25, wherein said catalytic effectiveness on d4T and ddT is at least 5 times greater than that of the native N-deoxyribosyl transferase protein of *L. fermentum* represented by SEQ ID NO: 2.

Claim 27 (Previously Presented): The protein according to claim 13, wherein the protein consists of a polypeptide of sequence SEQ ID NO: 4.

Claim 28 (Previously Presented): An isolated or purified nucleic acid that encodes the protein according to claim 13.

Claim 29 (Previously Presented): An expression vector comprising the nucleic acid according to claim 28.

Claim 30 (Previously Presented): The vector according to claim 29, further comprising a promoter effective in a eukaryotic or prokaryotic cell for expressing said nucleic acid.

Claim 31 (Previously Presented): The vector according to claim 29, which is a plasmid capable of transforming and being maintained in *E. coli*.

Claim 32 (Previously Presented): A host cell comprising a vector according to claim 29.

Claim 33 (Withdrawn): A method for transferring a dideoxyribose (ddR) from a dideoxynucleoside to another nucleoside, comprising:

contacting the dideoxynucleoside with a protein having an N-dideoxyribosyl transferase activity according to claim 13.

Claim 34 (Withdrawn): The method according to claim 33, further comprising synthesizing a 2',3'-dideoxynucleoside.

Claim 35 (Withdrawn): The method according to claim 33, further comprising synthesizing a 2',3'-didehydro-2',3'-dideoxynucleoside.

Claim 36 (Withdrawn): A method for preparing a nucleoside or a nucleotide analogue, comprising:

expressing the N-deoxyribosyl transferase protein (DTP) encoded by the the host cell according to claim 32 for a time and under conditions suitable for preparing a nucleoside or nucleotide analogue possessing an anti-tumor property.

Claim 37 (Withdrawn): The method according to claim 36, wherein said nucleoside or nucleotide analogue is ddI or ddC.

Claim 38 (Withdrawn): A method for preparing a compound comprising contacting a substrate with the protein according to claim 13.

Claim 39 (Withdrawn): The method according to claim 38, wherein said compound is a nucleoside or a nucleotide analogue useful for the treatment of cancer or an infectious disease a dideoxyribonucleoside, ddC, ddI or a didehydro-dideoxyribonucleoside.

Claim 40 (Previously Presented): A strain of *E. coli* deposited at the CNCM on 22nd March 2004 under accession number I-3192.